

Complete listing of all claims, with markings and status identifiers
(currently amended claims showing deletions by ~~strikethrough~~ and additions by underlining)

1. (Canceled)

2. (Canceled)

3. (Currently amended) A compound according to claim 2 of formula (I),

(R²R³)-A⁷-A⁸-A⁹-A¹⁰-A¹¹-A¹²-A¹³-A¹⁴-A¹⁵-A¹⁶-A¹⁷-A¹⁸-A¹⁹-A²⁰-A²¹-A²²-A²³-A²⁴-A²⁵-A²⁶-A²⁷-A²⁸-
A²⁹-A³⁰-A³¹-A³²-A³³-A³⁴-A³⁵-A³⁶-A³⁷-A³⁸-A³⁹-R¹

(I)

wherein

A⁷ is L-His, Ura, Paa, Pta, Amp, Tma-His, des-amino-His, or deleted;

A⁸ is Ala, β -Ala, Gly, Ser, D-Ala, Aib, Acc, N-Me-Ala, N-Me-D-Ala or N-Me-Gly;

A⁹ is Glu, N-Me-Glu or N-Me-Asp;

A¹⁰ is Gly, Acc, β -Ala or Aib;

A¹¹ is Thr;

A¹² is Phe, Acc, 1Nal, 2Nal, or Aic;

A¹³ is Thr;

A¹⁴ is Ser or Aib;

A¹⁵ is Asp;

A¹⁶ is Val, Acc or Aib;

A¹⁷ is Ser;

A¹⁸ is Ser or Lys;

A¹⁹ is Tyr, 1Nal or 2Nal;

A²⁰ is Leu, Acc or Cha;

A²¹ is Glu;

A²² is Gly, Acc, β -Ala, Glu or Aib;

A²³ is Gln or Glu;

A²⁴ is Ala, Aib or Acc;

A²⁵ is Ala, Aib, Acc, Lys, Arg, hArg, Orn, HN-CH((CH₂)_n-N(R¹⁰R¹¹))-C(O) or HN-CH((CH₂)_e-X³)-C(O);

A²⁶ is Lys, Arg, hArg, Orn, Lys(N^e-decanoyl)), HN-CH((CH₂)_n-N(R¹⁰R¹¹))-C(O) or HN-CH((CH₂)_e-X³)-C(O);

A²⁷ is Glu, Leu, Aib or Lys;

A²⁸ is Phe, 1Nal or 2Nal;

A²⁹ is Ile or Acc;

A³⁰ is Ala or Aib;

A³¹ is Trp, Phe, 1Nal or 2Nal;

A³² is Leu, Acc or Cha; and

A³³ is Val, Lys or Acc;

A³⁴ is Lys, Arg, hArg, Orn, HN-CH((CH₂)_n-N(R¹⁰R¹¹))-C(O) or HN-CH((CH₂)_e-X³)-C(O);

A³⁵ is β -Ala, D-Ala, Gaba, Ava, HN-(CH₂)_m-C(O), Aib, Acc, D-Arg or a D-amino acid;

A³⁶ is L- or D-Arg, D- or L-Lys, or Lys(N^e-decanoyl) or Lys(N^e-dodecanoyl) or D- or L-hArg, D- or L-Orn or HN-CH((CH₂)_n-N(R¹⁰R¹¹))-C(O), or HN-CH((CH₂)_e-X³)-C(O);

A³⁷ is Gly, β -Ala, Gaba, Aib, Acc, Act, Apc, Aun, Ava, Pro, Dhp, Dmt, Pip, L- or

D- Arg, L- or D- Asp or Glu, Lys(N^e-decanoyl), Lys(N^e-dodecanoyl), Lys(N^e-octanoyl), Lys(N^e-tetradecanoyl), or Ser(O-decanoyl);

A³⁸ is D- or L- His, L- or D-Ala, Asn, Gln, Ser, Thr, Acc, Ado, Aib, Apc, Act, Arg, Ava, Gly, β -Ala, Gaba, or HN-(CH₂)_s-C(O);

A³⁹ is D- or L- His, L- or D-Ala, Asn, Gln, Ser, Thr, Acc, Ado, Aib, Apc, Act, Arg, Aun, Gly, β -Ala, Gaba, Lys(N^e-octanoyl), HN-(CH₂)_s-C(O), or deleted;

R¹ is OH, NH₂; (C₁-C₃₀)alkoxy, or NH-X²-CH₂-Z⁰, wherein X² is a (C₀-C₂), (C₄-C₉) or (C₁₁-C₁₉)hydrocarbon moiety and Z⁰ is H, OH, CO₂H or CONH₂;

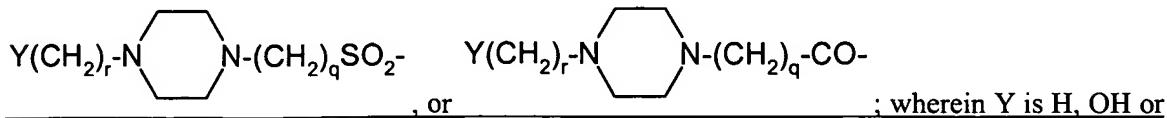
X³ is

or -C(O)-NHR¹², wherein X⁴ is, independently for each occurrence, -C(O)-, -NH-C(O)- or -CH₂-, and wherein f is, independently for each occurrence, an integer from 1 to 29 inclusive; each of R² and R³ is independently selected from the group consisting of H, (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, optionally substituted phenyl(C₁-C₃₀)alkyl, optionally substituted naphthyl(C₁-C₃₀)alkyl, hydroxy(C₁-C₃₀)alkyl, hydroxy(C₂-C₃₀)alkenyl, hydroxyphenyl(C₁-C₃₀)alkyl, and hydroxynaphthyl(C₁-C₃₀)alkyl;

wherein the phenyl group of said optionally substituted phenyl(C₁-C₃₀)alkyl moiety, and said naphthyl group of said optionally substituted naphthyl(C₁-C₃₀)alkyl moiety each is,

independently for each occurrence, substituted with 1 or more substituents selected, independently for each occurrence, from the group consisting of halo, OH, NH₂, NO₂ and CN;

or one of R² and R³ is (CH₃)₂-N-C=N(CH₃)₂, (C₁-C₃₀)acyl, (C₁-C₃₀)alkylsulfonyl, C(O)X⁵,



NH₂; r is 0 to 4; q is 0 to 4; and X⁵ is (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, phenyl(C₁-C₃₀)alkyl, naphthyl(C₁-C₃₀)alkyl, hydroxy(C₁-C₃₀)alkyl, hydroxy(C₂-C₃₀)alkenyl, hydroxyphenyl(C₁-C₃₀)alkyl or hydroxynaphthyl(C₁-C₃₀)alkyl;

X⁶, X⁷, X⁸, X⁹, X¹⁰ for each occurrence is independently selected from the group consisting of H, (C₁-C₆)alkyl, OH, OR⁴, NO₂, CN, and halo;

R⁴ is (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, phenyl(C₁-C₃₀)alkyl, naphthyl(C₁-C₃₀)alkyl, hydroxy(C₁-C₃₀)alkyl, hydroxy(C₂-C₃₀)alkenyl, hydroxyphenyl(C₁-C₃₀)alkyl or hydroxynaphthyl(C₁-C₃₀)alkyl;

e is, independently for each occurrence, an integer from 1 to 4 inclusive;

m is, independently for each occurrence, an integer from 5 to 24 inclusive;

s is, independently for each occurrence, an integer from 5 to 10 or from 12 to 20 inclusive;

n is, independently for each occurrence, an integer from 1 to 5, inclusive;

each of R¹⁰ and R¹¹ is, independently for each occurrence, H, (C₁-C₃₀)alkyl, (C₁-C₃₀)acyl, (C₁-C₃₀)alkylsulfonyl, -C((NH)(NH₂)) or



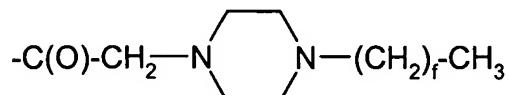
; and

R¹² and R¹³ each is, independently for each occurrence, (C₁-C₃₀)alkyl;

provided that:

when A⁷ is Ura, Paa or Pta, then R² and R³ are deleted;

when R¹⁰ is (C₁-C₃₀)acyl, (C₁-C₃₀)alkylsulfonyl, -C((NH)(NH₂)) or



, then R¹¹ is H or (C₁-C₃₀)alkyl;

(i) at least one amino acid of a compound of formula (I) is not the same as the native sequence of hGLP-1(7-38 or -39)NH₂ or hGLP-1(7-38 or -39)OH;

(ii) a compound of formula (I) is not an analogue of hGLP-1(7-38 or -39)NH₂ or hGLP-1(7-38, or -39)OH wherein a single position has been substituted by Ala;

(iii) a compound of formula (I) is not $(\text{Arg}^{26,34}, \text{Lys}^{38})\text{hGLP-1}(7-38)\text{-E}$, $(\text{Lys}^{26}(\text{N}^{\epsilon}\text{-alkanoyl}))\text{hGLP-1}(7-38)\text{-E}$, $(\text{Lys}^{34}(\text{N}^{\epsilon}\text{-alkanoyl}))\text{hGLP-1}(7-38)\text{-E}$, $(\text{Arg}^{26}, \text{Lys}^{34}(\text{N}^{\epsilon}\text{-alkanoyl}))\text{hGLP-1}(8-38)\text{-E}$, $(\text{Arg}^{26,34}, \text{Lys}^{36}(\text{N}^{\epsilon}\text{-alkanoyl}))\text{hGLP-1}(7-38)\text{-E}$ or $(\text{Arg}^{26,34}, \text{Lys}^{38}(\text{N}^{\epsilon}\text{-alkanoyl}))\text{hGLP-1}(7-38)\text{-E}$, wherein E is -OH or -NH₂;

(iv) a compound of formula (I) is not $Z^1\text{-hGLP-1}(7-38)\text{-OH}$, $Z^1\text{-hGLP-1}(7-38)\text{-NH}_2$; wherein Z^1 is selected from the group consisting of:

(a) $(\text{Arg}^{26}), (\text{Arg}^{34}), (\text{Arg}^{26,34}), (\text{Lys}^{36}), (\text{Arg}^{26}, \text{Lys}^{36}), (\text{Arg}^{34}, \text{Lys}^{36}), (\text{D-Lys}^{36}), (\text{Arg}^{36}), (\text{Arg}^{26,34}, \text{Lys}^{36})$ or $(\text{Arg}^{26,36}, \text{Lys}^{34})$;

(b) (Asp^{21}) ;

(c) at least one of $(\text{Aib}^8), (\text{D-Ala}^8)$ and (Asp^9) ; and

(d) $(\text{Tyr}^7), (\text{N-acyl-His}^7), (\text{N-alkyl-His}^7), (\text{N-acyl-D-His}^7)$ or (N-alkyl-D-His^7) ; and

(v) a compound of formula (I) is not a combination of any two of the substitutions listed in groups

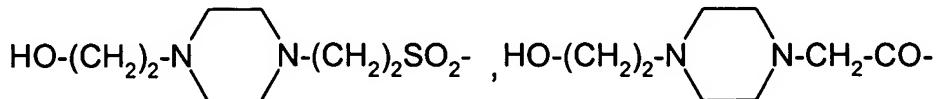
(a) to (d);

or a pharmaceutically acceptable salt thereof.

4. (Currently amended) A compound according to ~~claim 2~~ claim 3, wherein A⁸ is Ala, Gly, Ser, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala or N-Me-Gly; A¹⁰ is Gly; A¹² is Phe, 1Nal, 2Nal, A6c or A5c; A¹⁶ is Val, A6c or A5c; A²⁰ is Leu, A6c, A5c or Cha; A²² is Gly, β -Ala, Glu or Aib; A²⁴ is Ala or Aib; A²⁹ is Ile, A6c or A5c; A³² is Leu, A6c, A5c or Cha; A³³ is Val, Lys, A6c or A5c; A³⁵ is Aib, β -Ala, Ado, A6c, A5c, D-Arg or Acc; A³⁷ is Gly, Aib, β -Ala, D-Ala, Pro, Asp, Aun or D-Asp; A³⁸ is D- or L- His, Asn, Ser, Apc, Act, Gly, β -Ala or Gaba; and A³⁹ is Ser, Thr or Aib; or a pharmaceutically acceptable salt thereof.

5. (Original) A compound according to claim 4 or a pharmaceutically acceptable salt thereof, X⁴ for each occurrence is -C(O)-; and R¹ is OH or NH₂; or a pharmaceutically acceptable salt thereof.

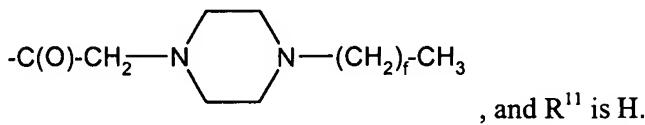
6. (Original) A compound according to claim 5 or a pharmaceutically acceptable salt thereof, wherein R² is H and R³ is (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, (C₁-C₃₀)acyl, (C₁-C₃₀)alkylsulfonyl,



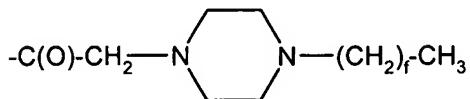
or



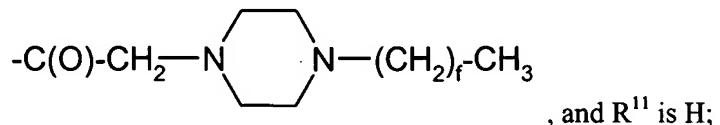
7. (Original) A compound according to claim 5 or a pharmaceutically acceptable salt thereof, wherein R¹⁰ is (C₁-C₃₀)acyl, (C₁-C₃₀)alkylsulfonyl or



8. (Original) A compound according to claim 7 or a pharmaceutically acceptable salt thereof, wherein R¹⁰ is (C₄-C₂₀)acyl, (C₄-C₂₀)alkylsulfonyl or

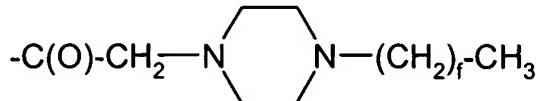


9. (Currently amended) A compound according to ~~claim 2~~ claim 3, wherein: A⁸ is Ala, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala or N-Me-Gly; A¹⁰ is Gly; A¹² is Phe, 1Nal, 2Nal, A6c or A5c; A¹⁶ is Val, A6c or A5c; A²⁰ is Leu, A6c, A5c or Cha; A²² is Gly, β -Ala, Glu or Aib; A²⁴ is Ala or Aib; A²⁹ is Ile, A6c or A5c; A³² is Leu, A6c, A5c or Cha; A³³ is Val, Lys, A6c or A5c; A³⁵ is Aib, β -Ala, Ado, A6c, A5c or D-Arg; and A³⁷ is Gly, Aib, β -Ala, D-Ala, Pro or D-Asp; A³⁸ is D- or L- His, Asn, Ser, Gly, β -Ala or Gaba; and A³⁹ is Ser, or deleted; X⁴ for each occurrence is -C(O)-; e for each occurrence is independently 1 or 2; R¹ is OH or NH₂; R¹⁰ is (C₁-C₃₀)acyl, (C₁-C₃₀)alkylsulfonyl or



or a pharmaceutically acceptable salt thereof.

10. (Original) A compound according to claim 9, wherein R¹⁰ is (C₄-C₂₀)acyl, (C₄-



C₂₀)alkylsulfonyl or , or a pharmaceutically acceptable salt thereof.

11. (Currently amended) A compound according to ~~claim 2~~ claim 3 wherein said compound is according to the formula:

(Aib^{8,35}, Arg^{26,34}, Phe³¹, Pro³⁷, Ser^{38,39})hGLP-1(7-39)-NH₂; (SEQ ID NO:1)
(Aib^{8,35,37}, Arg^{26,34}, Phe³¹, Asn³⁸)hGLP-1(7-38)-NH₂; (SEQ ID NO:2)
(Aib^{8,35,37}, Arg^{26,34}, Phe³¹, Ser³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:3)
(Aib^{8,35,37}, Gaba³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:4)
(Aib^{8,35,37}, Arg^{26,34}, Phe³¹, His³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:5)
(Aib^{8,35}, Arg^{26,34}, Phe³¹, β-Ala³⁷, His³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:6)
(Aib^{8,35,37}, Arg^{26,34}, D-His³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:7)
(Aib^{8,35,37}, β-Ala³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:8)
(Aib^{8,35}, Arg^{26,34}, β-Ala³⁷, His³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:9)
(Aib^{8,35,37}, Arg^{26,34}, Phe³¹, Gly³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:10)
(Aib^{8,35,37}, Arg^{26,34}, Gly³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:11)
(Aib^{8,35,37}, Arg^{26,34}, β-Ala³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:12)
(Aib^{8,35,37}, Arg^{26,34}, Gaba³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:13)
(Aib^{8,35,37}, Arg³⁴, Phe³¹, His³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:14)
(Aib^{8,35,37}, Arg^{26,34}, His³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:15)
(Aib^{8,35,37}, Arg^{26,34}, Phe³¹, Gaba³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:16)
(Aib^{8,35,37}, Arg^{26,34}, Phe³¹, Ava³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:17)
(Aib^{8,35,37}, Arg^{26,34}, Ava³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:18)
(Aib^{8,35,37}, Arg³⁴, Phe³¹, D-His³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:19)
(Aib^{8,35,37}, Arg³⁴, Phe³¹, Gly³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:20)
(Aib^{8,35,37}, Gly³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:21)
(Aib^{8,35,37}, Arg^{26,34}, Phe³¹, D-His³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:22)
(Aib^{8,35}, Arg^{26,34}, Phe³¹, β-Ala³⁷, D-His³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:23)
(Aib^{8,35,37}, Arg^{26,34}, Phe³¹, β-Ala³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:24)
(Aib^{8,35}, Arg^{26,34}, Phe³¹, β-Ala^{37,38})hGLP-1(7-38) NH₂; (SEQ ID NO:25)

(Aib^{8,35,37}, Arg³⁴, Phe³¹, β -Ala³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:26) or
(Aib^{8,35,37}, Arg³⁴, Phe³¹, Gaba³⁸)hGLP-1(7-38) NH₂; (SEQ ID NO:27)
or a pharmaceutically acceptable salt thereof.

12. (Currently amended) A pharmaceutical composition comprising ~~an effective amount~~
of a compound according to ~~claim 2~~ claim 3 or a pharmaceutically acceptable salt thereof and a
pharmaceutically acceptable carrier or diluent.

13. (Canceled)

14. (Currently amended) A method of treating a disease selected from the group
consisting of Type I diabetes[[],] and Type II diabetes, ~~obesity, glucagonomas, secretory~~
~~disorders of the airway, metabolic disorder, arthritis, osteoporosis, central nervous system~~
~~disease, restenosis, neurodegenerative disease, renal failure, congestive heart failure, nephrotic~~
~~syndrome, cirrhosis, pulmonary edema, hypertension, treatment of respiratory distress, disorders~~
~~wherein the reduction of food intake is desired, hypoglycemia and malabsorption syndrome~~
~~associated with gastrectomy or small bowel resection~~, in a subject in need thereof which
comprises administering to said subject an effective amount of a compound according to ~~claim 2~~
claim 11 or a pharmaceutically acceptable salt thereof.

15-27. (Canceled)